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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/743,557	12/22/2003	Khalid K. Sadozai	0103343.00128US1	5063

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EXAMINER	
BROWN, COURTNEY A	
ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
06/10/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/743,557	SADOZAI ET AL.	
	Examiner	Art Unit	
	COURTNEY BROWN	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *1-10 and 23-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/21/2004,9/30/2004, and 3/6/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments/Remarks filed on February 1, 2008 is acknowledged. Claims 1-48 are pending. Claims 1-10 and 23-48 are withdrawn as being directed to a non-elected invention. Claims 11-22 are being examined for patentability.

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Information Disclosure Statement

The Information Disclosure Statements (IDS) submitted on June 21, 2004, September 30, 2004, and March 6, 2008 are being considered by the examiner.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11, 13, 14, 17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al. (US Patent Application 2002/0049281 A1) in view of Prestwich et al. (European Patent Application 0416205 A2).

Applicant's Invention

Applicant claims a method of augmenting tissue in a human in need comprising the use of a hyaluronic acid (HA) composition that includes cross-linked, water-insoluble hydrated hyaluronic acid gel particles. These particles have a preferred diameter between about 20 μm to about 1000 μm wherein the distribution of the said particles is a multimodial distribution. The cross linkage of the particle may be performed with different compounds such an optionally substituted o-acyl isourea or N-acyl urea. The said composition may further comprise a local anesthetic, specifically lidocaine HCI. Additionally, the claimed method comprises the administration of the hyaluronic acid composition by forceful needle injection into a human at the location needing tissue augmentation.

Determination of the scope and the content of the prior art (MPEP 2141.01)

Zhao et al. teach that cross-linked HA derivatives may be used in a variety of forms including beads ([0088], claims 11, 17, and 19 of instant application), and are useful in hard and soft tissue augmentation [0085], claims 11, 17, and 19 of instant application) and for delivery of therapeutically active agents such as anti-inflammatory agents, antibiotics, analgesics, and wound healing promoters ([0086], claims 13 and 14 of instant application).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the invention of the instant application and that of Zhao et al. is that the instant invention requires cross linkage of the HA hydrated gel particles performed with an optionally substituted o-acyl isourea or N- acyl urea as opposed to the use of multiple cross-linked derivatives of HA. For this reason, the teaching of Prestwich et al. is joined. Prestwich et al. teach that the preparation of N-acylurea and O-acylisourea derivatives of HA that are useful in wound healing (abstract, claim 11 of instant application).

Finding of prima facie obviousness

Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the two cited references to arrive at a method of augmenting tissue in a human in need comprising the use of a cross-linked hyaluronic acid (HA) composition. Zhao et al. teach the process for cross-linking hylauronic acid to polymers along with their use in tissue augmentation and Prestwhich et al. teach the preparation of N-Acylureas and O-acylisourea hyaluronic acid derivatives. One would have been motivated to make this combination in order to receive the expected benefit of having an alternative method of introducing and controlling the release of lidocaine HCl (see page 2, lines 41-55 to page 3, lines 1-16 of Prestwich et al.). “It would be

prima facie obvious to combine two methods each of which is taught by the prior art to be useful for the same purpose in order to form a resultant method that is to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in prior art." In re Kerkhoven, 205 USPQ 1069 (C.C.P.A. 1980).

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Claims 11,12, 13, 14, 17, 19, and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al. (US Patent Application 2002/0049281 A1) in view of Duranti (Dermatologic Surgery) and further in view of Lawin et al. (WO/9602209 A1).

Determination of the scope and the content of the prior art (MPEP 2141.01)

The teachings of Zhao et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the invention of the instant application and that of Zhao et al. is that the instant invention requires hyaluronic acid (HA) composition that can be injected and comprises cross-linked, water- insoluble hydrated hyaluronic acid gel

particles that have a preferred diameter between about 20 μm to about 1000 μm wherein the distribution of the said particles is a multimodial distribution. For this reason, the teachings of Durantiet al. and Lawin et al. are joined.

Duranti et al. teach that when hyaluronic acid chains are chemically cross-linked, the solubility and the rheological properties of the material change to become more viscous and water-insoluble gels (see page 1317, claim 11 of instant application). Duranti et al. teach that hyaluronic acid gel is versatile enough to be injected through 27 or 30 gauge needles (see page 1323, discussion section, claim 11 of instant application). Additionally, Duranti et al. teach that the low viscosity of HA at high shear rates facilitate its injection when forced through a needle and its high viscosity at low shear rates (when stationary) allows a long residence in the tissues (see page1324, claims 20-22 of instant application).

Lawin et al. teach the use of an injectable biocompatible composition consisting of particles that range in size from 100 to 1,000 microns (see page 2, claims 17 and 20-22 of instant application). Lawin et al. also teach the use of hyaluronic acid as a carrier solution or suspension (see claim 12 of reference, claim 11 of instant application).

Finding of prima facie obviousness

Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the cited references to arrive at a method of augmenting tissue in a human in need comprising the use of a cross-linked hyaluronic

acid (HA) composition. Zhao et al. teach the process for cross-linking hylauronic acid to polymers along with their use in tissue augmentation. Duranti et al. teach the use of HA gel particles and the administration of the hyaluronic acid composition by forceful needle injection along with the importance of the HA composition's viscosity. Lawin et al. teach the use of particles that range in size from 100 to 1000 microns. One would have been motivated to make this combination in order to receive the expected benefit of a cross-linked HA gel that has slow digestion and a high, almost plastic viscosity when stationary making it sort of etiologic therapy of the aging face (see Duranti et al., page 1325). One would also have been motivated to make this combination in order to receive the expected benefit of an injectable composition of appropriately sized particles to be delivered into the body to a tissue site through a small-bore instrument to strengthen, bulk-up, and augment the tissue site and surrounding area (see Lawin et al., paragraph 1 of background section, claims 11 and 12 of instant application). It would be prima facie obvious to combine two methods each of which is taught by the prior art to be useful for the same purpose in order to form a resultant method that is to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in prior art." In re Kerkhoven, 205 USPQ 1069 (C.C.P.A. 1980).

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Claims 11, 13-19, and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhao et al. (US Patent Application 2002/0049281 A1) in view of Chasin et al. (US Patent 5,942,241).

Determination of the scope and the content of the prior art (MPEP 2141.01)

The teachings of Zhao et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed above.

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

The difference between the invention of the instant application and that of Zhao et al. is that the instant invention requires that the HA composition include lidocaine HCL as a bioactive agent. For this reason, the teaching of Chasin et al. is joined. Chasin et al. teach the use of a local anesthetic such as lidocaine (see claim 8 of reference, claim 13-16 if instant application) that can be formulated in injectable microspheres in combination with at least one augmenting agent (column 10, lines 20-24, claims 13-16 of instant application). Chasin et al. also teach the use of hyaluronic acid as a preferred controlled release material (column 12, lines 43-56, claim 11 of instant application).

Finding of prima facie obviousness

Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the two cited references to arrive at a method of augmenting tissue in a human in need comprising the use of a cross-linked hyaluronic acid (HA) composition Zhao et al. teach the process for cross-linking hylauronic acid to

polymers along with their use in tissue augmentation and Chasin et al. teach the use of a local anesthetic. One would have been motivated to make this combination in order to receive the expected benefit of using a local anesthetic such as lidocaine to eliminate discomfort at the injection site (see Duranti et al., page 1325) "It would be prima facie obvious to combine two methods each of which is taught by the prior art to be useful for the same purpose in order to form a resultant method that is to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in prior art." In re Kerkhoven, 205 USPQ 1069 (C.C.P.A. 1980).

Claims 17, 18, and 20-22 are drawn to physical properties of the HA formulation. One of ordinary skill in the art would expect that the claimed formulation would behave wherein the distribution is a multimodal distribution and posses a storage modulus G' of at least 400 Pa and a kinematic viscosity of at least 100 Pa.

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Examiner's Response to Applicant's Arguments

Applicant's arguments with respect to claims 11-22 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

None of the claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR Only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electron Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Courtney Brown, whose telephone number is 571-270-3284. The examiner can normally be reached on Monday-Friday from 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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